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Differential effects of local application of BMP-2 or TGF-beta 1 on both articular cartilage composition and osteophyte formation.

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OBJECTIVE: The related molecules bone morphogenetic protein-2 (BMP-2) and transforming growth factor beta-1 (TGF-beta 1) have both been shown to stimulate chondrocyte proteoglycan (PG) synthesis in vitro. We investigated the in-vivo effects of these factors on articular cartilage PG metabolism. **DESIGN:** Several doses of BMP-2 or TGF-beta 1 were injected into the murine knee joint, once or repeatedly. Patellar cartilage PG synthesis was measured by [35S]-sulfate incorporation and reverse transcriptase polymerase chain reaction (RT-PCR). PG content was analyzed by measuring safranin O staining intensity on histologic sections. **RESULTS:** A single injection of 200 ng BMP-2 induced a much earlier and more impressive stimulation of articular cartilage PG synthesis, than 200 ng TGF-beta 1. RT-PCR revealed that both factors upregulated mRNA of aggrecan more than that of biglycan and decorin. However, 21 days after a single injection of 200 ng TGF-beta 1 PG synthesis still was significantly increased, while stimulation by BMP-2 only lasted for 3 to 4 days. Stimulation by BMP-2 could be prolonged to at least 2 weeks by triple injections of 200 ng each, at alternate days. Remarkably, even after this intense exposure to BMP-2, stimulation of PG synthesis was not reflected in long-lasting enhancement of PG content of articular cartilage. In contrast, even a single injection with 200 ng of TGF-beta 1 induced prolonged enhancement of PG content. After repeated injections, both BMP-2 and TGF-beta 1 induced chondrogenesis at specific sites. 'Chondrocytes' induced by BMP-2 were found predominantly in the region where the

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growth plates meet the joint space, while those triggered by TGF-beta 1 originated from the periosteum also at sites remote from the growth plates. CONCLUSIONS: BMP-2 and TGF-beta stimulate PG synthesis and PG content with different kinetics, and these factors have different chondro-inductive properties.

PMID: 10197165 [PubMed - indexed for MEDLINE]

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